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REPORT NO. T4-90

RELIABILITY OF PATTERN REVERSAL EVOKED POTENTIALS (PREP) USING THE NICOLET PATHFINDER II

U S ARMY RESEARCH INSTITUTE
OF
ENVIRONMENTAL MEDICINE
Natick, Massachusetts

FEBRUARY 1990

UNITED STATES ARMY
MEDICAL RESEARCH & DEVELOPMENT COMMAND

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SECURITY CLASSIFICATION OF THIS PAGE

REPORT DOCUMENTATION PAGE

Form Approved OMB No. 0704-0188

1a. REPORT SECURITY CLASSIFICATION Unclassified	1b. RESTRICTIVE MARKINGS
2a. SECURITY CLASSIFICATION AUTHORITY	3. DISTRIBUTION/AVAILABILITY OF REPORT Approved for public release; distribution is unlimited
2b. DECLASSIFICATION/DOWNGRADING SCHEDULE	
4. PERFORMING ORGANIZATION REPORT NUMBER(S) T4-90	5. MONITORING ORGANIZATION REPORT NUMBER(S)
6a. NAME OF PERFORMING ORGANIZATION US Army Research Institute of Environmental Medicine 6b. OFFICE SYMBOL (If applicable) SGRD-UE-HP	7a. NAME OF MONITORING ORGANIZATION US Army Medical Research & Development Command
6c. ADDRESS (City, State, and ZIP Code) Natick, MA 01760-5007	7b. ADDRESS (City, State, and ZIP Code) Ft. Detrick, Frederick, MD 21701-5012
8a. NAME OF FUNDING/SPONSORING ORGANIZATION Same as 6a. 8b. OFFICE SYMBOL (If applicable)	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER
8c. ADDRESS (City, State, and ZIP Code) Same as 6c.	10. SOURCE OF FUNDING NUMBERS PROGRAM ELEMENT NO. 63002A PROJECT NO. 3M2630-02D995 TASK NO. AE WORK UNIT ACCESSION NO. DA305221

11. TITLE (Include Security Classification)

Reliability of Pattern Reversal Evoked Potentials (PREP) Using the NICOLET Pathfinder II

12. PERSONAL AUTHOR(S)

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13a. TYPE OF REPORT	13b. TIME COVERED	14. DATE OF REPORT (Year, Month, Day)	15. PAGE COUNT
Technical Report	FROM 11/88 TO 2/90	1990 February 21	40

16. SUPPLEMENTARY NOTATION

17. COSATI CODES			18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)
FIELD	GROUP	SUB-GROUP	Evoked Potential, Pattern Reversal Evoked Potential, Evoked Response, Nicolet Pathfinder, JWGD 3 MILPERF Tag Level 1, PREP Baseline Norms

19. ABSTRACT (Continue on reverse if necessary and identify by block number)

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Signal averaging systems such as the Nicolet Pathfinder II extract the EP from the background electroencelphogram. Because different laboratories may have slightly different techniques and environmental conditions, each laboratory first must establish normative values for the system before research studies can be undertaken.

The purposes of this study were to assess the reliability of our system for the collection of PREPs and to establish laboratory norms. Twenty-four males and eleven females served as volunteer research subjects. Subjects were administered two trials for each eye on each

20. DISTRIBUTION/AVAILABILITY OF ABSTRACT	21. ABSTRACT SECURITY CLASSIFICATION	
☒ UNCLASSIFIED/UNLIMITED ☐ SAME AS RPT. ☐ DTIC USERS	Unclassified	
22a. NAME OF RESPONSIBLE INDIVIDUAL Terry M. Rauch, MAJ, MS	22b. TELEPHONE (Include Area Code) (508) 651-4195	22c. OFFICE SYMBOL SGRD-UE-HP

DD Form 1473, JUN 86 *Previous editions are obsolete.*

SECURITY CLASSIFICATION OF THIS PAGE

UNCLASSIFIED

19. ABSTRACT (Continued)

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The latencies of the two negative waveforms $\overline{N75}$ and $\overline{N145}$ as well as the positive peak $\overline{P100}$ were assessed for replicability. Amplitudes from $\overline{N75}$-$\overline{P100}$ and from $\overline{P100}$-$\overline{N145}$ were also examined. Gender differences were noted. Means were calculated and established to use as norms for the new laboratory.

A repeated measures analysis of variance (ANOVA) and an intraclass reliability analysis were performed. The ANOVA assessed differences over days and between males and females. Intraclass reliability assessed error variances due to trials, days, and subjects. Latencies and amplitudes proved reliable and replicable for recording sites F_{pz}-O_z and F_{pz}-O_2. Females had significantly shorter $\overline{P100}$ latencies and greater amplitudes than males.

The results from this study are comparable to other laboratories engaged in EP research. The Nicolet Pathfinder II is considered to be a reliable system in our laboratory for collecting PREPs.

Brain evoked responses have traditionally been used for neurodiagnostic purposes in the clinical setting. A novel utilization of evoked potential technology enables the systematic correlation of changes in the performance of cognitive and/or sensorimotor tasks to changes in the amplitude and latency of neuronal signals in specific pathways within the brain. Such performance assessment technology represents the only window to the human central nervous system with direct application to the performance of military skills.

The views, opinions and/or findings contained in this report are those of the authors and should not be construed as an official Department of the Army position, policy or decision, unless so designated by other official documentation.

Human subjects participated in this study after giving their free and informed voluntary consent. Investigators adhered to AR 70-25 and USAMRDC Regulation 70-25 on Use of Volunteers in Research.

ACKNOWLEDGEMENTS

We would like to thank Lynn Sleeper of Harvard University for providing valuable statistical assistance, Rebecca Kittredge for her assistance in the data reduction, and Everett Harman for review of the manuscript.

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TECHNICAL REPORT
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February 1990

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FOREWORD

The following project was conducted under the guidance of the Tri-Service Joint Working Group on Drug Dependent Degradation in Military Performance (JWGD3 MILPERF) as part of the Task Area Group (TAG) Level I. The main purpose of the TAG Level I is to identify adverse drug effects on neurological functions in order to provide guidance to other performance related TAG Levels. One goal of TAG Level I is the development of an automated, standardized and clinically relevant assessment of nervous system integrity. This will be achieved through the creation of the Neurophysiological Performance Assessment Battery (NP-PAB), consisting of a set of eight evoked potential protocols. Before the NP-PAB can be fully implemented, standardization of the test procedures must be accomplished. Then validation of the NP-PAB with two classes of antihistimines will proceed, using the standardization procedures, by a network of laboratories. This will result in a common archive for JWGD3 MILPERF related data.

Several different evoked potential assessment systems are in use by the laboratories in the JWGD3 MILPERF network. Standardization of the procedures will insure that similar results can be produced by different systems in different laboratory settings. The Health and Performance Division at the US Army Research Institute of Environmental Medicine was requested to participate in this validation effort by assessing three of the standardized procedures on the Nicolet Pathfinder II. Testing the ability of this system and laboratory setting to validate previous findings is the first step in the effort towards the standardization of the NP-PAB. A database of normal values for the

evoked potential laboratory at USARIEM will also be established. The second step, validation of the NP-PAB with two classes of antihistimines, may then proceed.

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ABSTRACT

Evoked potentials (EPs) are emerging as a useful tool to determine the functional integrity of the central and peripheral nervous systems. The Pattern Reversal Evoked Potential (PREP) provides an assessment of the functioning of the visual nervous system pathway.

Signal averaging systems such as the Nicolet Pathfinder II extract the EP from the background electroencephalogram. Because different laboratories may have slightly different techniques and environmental conditions, each laboratory first must establish normative values for the system before research studies can be undertaken.

The purposes of this study were to assess the reliability of our system for collection of PREPs and to establish laboratory norms. Twenty-four males and eleven females served as volunteer research subjects. Subjects were administered two trials for each eye on each of two days. Conditions remained constant for all trials. Using the International Electrode Placement System, surface electrodes were placed at C_z, O_z, O_1, O_2, and F_{pz}. Two sets of 100 pattern reversals were presented at the rate of 1.7/sec. A 32 square checkerboard pattern on a 12 inch TV monitor was used as the stimulus source.

The latencies of the two negative waveforms $\overline{N75}$ and $\overline{N145}$ as well as the positive peak $\overline{P100}$ were assessed for replicability. Amplitudes from $\overline{N75}$-$\overline{P100}$ and from $\overline{P100}$-$\overline{N145}$ were also examined. Gender differences were noted. Means were calculated and established to use as norms for the EP laboratory.

A repeated measures analysis of variance (ANOVA) and an intraclass reliability analysis were performed. The ANOVA assessed differences over days and between males and females. Intraclass reliability assessed error variances due to trials, days, and subjects. Latencies and amplitudes proved reliable and replicable for recording sites F_{pz}-O_z, and F_{pz}-O_2. Females had significantly shorter $\overline{P100}$ latencies and greater amplitudes than males.

The results from this study are comparable to other laboratories engaged in EP research. The Nicolet Pathfinder II is considered to be a reliable system in our laboratory for collecting PREPs.

Brain evoked responses have traditionally been used for neurodiagnostic purposes in the clinical setting. A novel utilization of evoked potential technology enables the systematic correlation of changes in the performance of cognitive and/or sensorimotor tasks to changes in the amplitude and latency of neuronal signals in specific pathways within the brain. Such performance assessment technology represents the only window to the human central nervous system with direct application to the performance of military skills.

Introduction

Electroencephalograms (EEG's) have long been used to record spontaneous and/or background activity of the brain. Differences in electrical potentials resulting from the ionic current flow across membranes, produce the different waves found in EEG's. Evoked responses obtained directly from the eye were first reported by Holmgren in 1865 (Celesia, 1985). The stimuli for these responses were bright flashes and the resultant evoked potentials (EPs) were several hundred microvolts (uV) in amplitude. This type of EP is called an electroretinogram (ERG).

Recently, EPs have emerged as a useful tool in assessing functional integrity of the central and peripheral nervous systems. Since the voltage from the visual EP ([flash] visual evoked response (VER) and pattern reversal evoked potential (PREP)) obtained from recordings on the scalp is very small (.5 to 20 uV) compared to background EEG voltage (up to 200 uV depending on the EEG rhythm) it is necessary to extract the EP from the background EEG (Best & Taylor, 1973). The evoked potential is "time-locked" to the stimulus, occurring at a specific time after stimulus presentation. It has been found that latencies of responses to these stimuli are nearly constant not only with the same subject across time, but also between different non-impaired subjects. Since the EP is the only aspect of the EEG which is stimulus dependent, the EP can be extracted from other brain activity through signal averaging. Successive evoked responses are digitized and added to the previous responses. After each addition, the sums are divided by the number of responses collected to produce a running average until the desired number of

responses have been collected. Successive averages are used to obtain a clean, well defined signal.

Several signal-averaging systems have been designed specifically for the collection of EPs. Attention to the technical specifications and proper calibration of the system help to insure that the system is reliable. However, slight variations may still exist between different types of systems, and even between different units of the same system. Further variations can occur in procedure or laboratory locations. Many researchers (Chiappa, 1983; Colon, Visser, deWeerd and Zonnerveldt, 1983; and Spehlman, 1985) strongly recommend that a new EP laboratory establish a normative database for each procedure to be used. Evoked potential data from other laboratories may be used initially as a reference standard. However, once normative data from the laboratory have been established, that data should be used in future studies conducted in that laboratory. To make comparisons with other laboratories, the normative values should replicate those of the reference laboratory. Spehlman (1985) recommends that 95 percent of the subjects tested in the new laboratory fall within the limits derived from the reference laboratory before the results should be considered replicated.

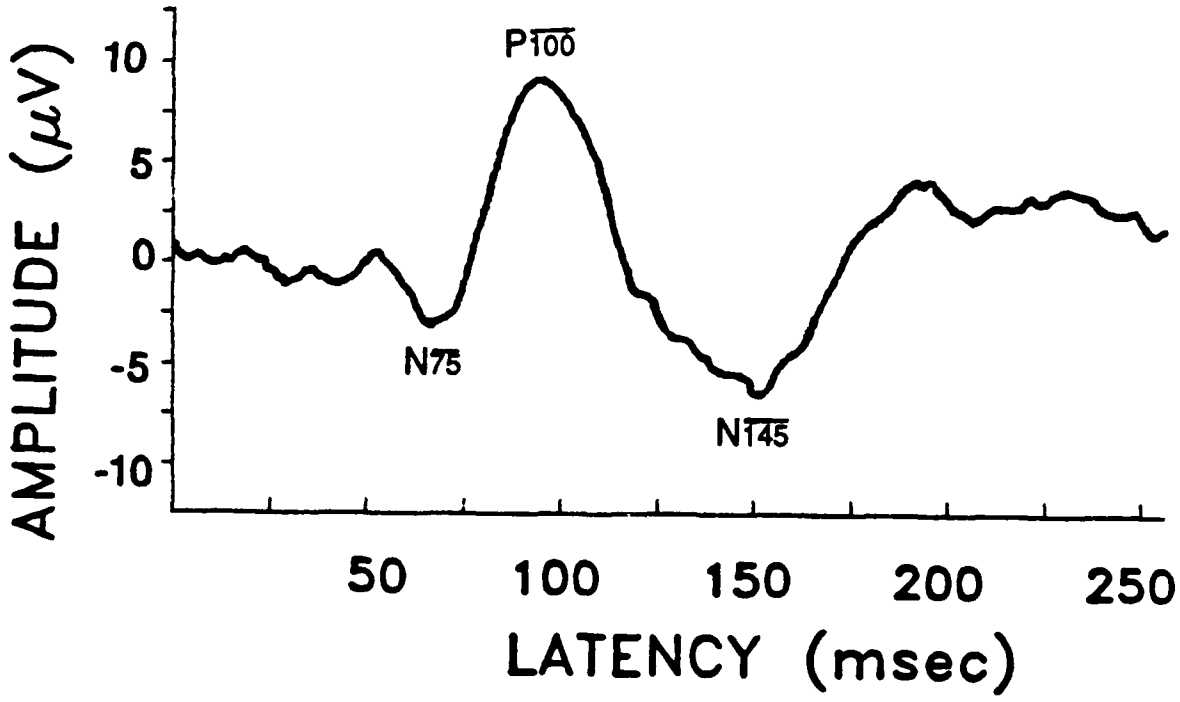
The visual EP provides a measure of integrity of the visual pathway (optic nerve function) and neuronal conduction velocity within the central nervous system structures concerned with visual information processing (AEEGS, 1984). Originally, visual EPs were obtained by stimulating with bright light flashes. A flash stimulus is still used with certain populations (e.g. infants, mentally impaired and coma patients) because these individuals cannot fixate on a TV monitor which

is necessary when using a pattern reversal stimulus. Using a flash does not require patient cooperation. It is not the stimulus of choice, however, because as Ciganek (1975) states: "though most intensively studied, the [flash] visual evoked response (VER) is very difficult to interpret." In addition, differences between what is normal and what is not has been difficult to establish (Celesia, 1985). Hubel and Wiesel (1959, 1974) found the visual system responds with a high specificity of the cortical neurons when stimulated by shapes. Over the past decade these findings have led to stimulation of the visual system using specific patterns. Most frequently used is the visual presentation of a reversing pattern of black and white checks. This type of stimulation is referred to as the pattern reversal evoked potential (PREP). The PREP wave has three major components. The most important being a positive peak occurring at approximately 100 msec (known as P1 or $\overline{P100}$) after stimulus presentation. The latencies of the two negative peaks or "valleys" of normal subjects are $\overline{N75}$, (N1), and $\overline{N145}$, (N2), (AEEGS, 1984). Figure 1 is an example of a PREP waveform whose origin is in the visual cortex. As is the the case with most EPs the exact origin is undetermined. The primary visual cortex on the medial surface as well as the secondary visual cortex on the lateral surface are thought to contribute but to an unknown extent (Spehlman, 1985). In general, cortical EPs are due largely to the spatial and temporal summation of post synaptic potentials generated at the membrane of nerve cell bodies and dendrites in response to the stimulus (Spehlman, 1985). It is believed that $\overline{P100}$ results from primary activation of the neurons in the striate and prestriate regions of the occipital cortex (Broadman's

FIGURE 1

PREP WAVEFORM KEY COMPONENTS

N$\overline{75}$, P$\overline{100}$, N$\overline{145}$



cortical area 19) and also from subsequent thalamocortical volleys (Chippa, 1983).

The purpose of this study was twofold. The test-retest reliability of a newly acquired Nicolet Pathfinder II (Nicolet Biomedical Instruments: Madison WI) in the environment of USARIEM's Evoked Potential Laboratory was assessed. Secondly, a normative PREP database for the laboratory was established.

METHOD

Subjects

Subjects were 24 male and 11 female USARIEM civilian and military personnel, between the ages of 20 and 39 years with normal or correctable vision (20/20 Snellen). The $\overline{P100}$ latency of subjects accepted for the database was required to fall within 2.5 standard deviation units of the norms determined by our reference laboratories (Colon, et al., 1983; and Chiappa, 1983).

Procedure

Testing occurred over two days following the same procedure. The PREP does not vary significantly over a few hours, days, or even several months in normal subjects. Stringent scheduling of the two test days was not necessary, however subjects were tested with two to seven days in between sessions. Each test session took approximately 20 minutes. The basic procedure used to collect PREP data in our laboratory was drawn directly from the procedure protocol published by Nicolet Biomedical

Instruments (1987) and is also the procedure standardized by the JWGD3 MILPERF Level I TAG (Reeves et al., 1990). All data was collected using the Nicolet Pathfinder II (Madison, WI), a neurodiagonostic system for the collection of evoked potentials. The Nicolet Pathfinder II is a self-contained system, including the electrode board, amplifier, stimuli and stimuli controls, memory blocks for recording and displaying waveforms, and waveform analysis.

The 10-20 International Electrode Placement System was utilized to insure that electrodes were placed in the same locations over repeated trials (Jasper, 1958). Surface electrodes were applied to the scalp at five sites: the vertex C_z; three occipital sites; O_1, O_z, and O_2; and at F_{Pz}. F_{Pz} served as the reference electrode with O_1, O_2, and O_z as the active electrodes. C_z was the ground electrode.

To minimize interference in the recorded signal the electrode site was prepared using an abrasive solution, Omni-Prep (D.O. Weaver & Co.; Aurora, CO) to remove oils and dead skin. Medi-Trace EEG Sol (Graphic Controls Corp.; Buffalo, NY) electrode cream was then used to adhere the electrode to the prepared site and provide clear electrical conduction.

The resistance to current flow, known as impedance, is in part a measure of the quality of the electrode-scalp interface. Impedance of the electrode-scalp connection, measured with an impedance meter on the Nicolet Pathfinder II, was required to be between one and five kilohoms to avoid excessive artifact.

Two trials were performed monocularly on each eye. The left eye was always recorded first. The non-stimulated eye was covered with an eye patch (covered with a sterile gauze pad) while data were being

collected on the stimulated eye. Stimulation was presented to the eye in the form of a reversing checkerboard pattern on a Nicolet NIC 1015 Pattern Reversal Stimulator with a 12 inch screen monitor positioned at eye level one meter in front of the subject. If the subject used corrective lenses, the lenses were worn during testing. The stimulus pattern consisted of a 32 square black and white checkerboard. The pattern was set to reverse 1.7 times per second. Two sets of 100 responses each were collected from the left eye, with the subject closing his/her eyes for two minutes between sets for rest. The patch was then switched to the left eye and the procedure repeated for two more sets of 100 responses from the right eye. Sensitivity was set to 50 uV and bandpass filters set at 1 HZ (low bandpass) and 100 HZ (high bandpass), to filter out undesired signals. The Pathfinder intrinsically filters out signals which appear to be muscle artifacts, obtaining 100 acceptable responses per trial. Subjects relaxed in an easy chair in an upright sitting position during data collection. They were instructed to fixate on a paper adhesive dot in the center of the video screen and refrain from excessive blinking. All data collection occurred in the dimly lit EP laboratory at USARIEM. Environmental conditions such as lighting, temperature, and stimulus intensity remained similar between trials.

Analysis

For PREP waveform analysis, the most important measure is peak latency of $\overline{P100}$. Also important is the amplitude from valley to peak for the preceding $\overline{N75}$ wave to the $\overline{P100}$ peak (AEEGS, 1984). Abnormal waves are considered to be those where a response is absent or there is a

prolonged $\overline{P100}$ peak latency, i.e. greater than 2.5 standard deviation units from the mean. No wave amplitude or latencies of the other waves, $\overline{N75}$ and $\overline{N145}$, need be considered for a normal wave if $\overline{P100}$ is normal. The latter measures are only examined if the $\overline{P100}$ latency is greater than 2.5 standard deviation units from the mean of our reference laboratory. Values for all waves were obtained directly from the Pathfinder using Nicolet software and a moving cursor which allows for marking waves on the Pathfinder CRT screen. Reliability of the various latency and amplitude measures is necessary before further analysis is appropriate. Proven reliability allows for future analysis of the effects of various treatments. Reliability estimates deal with both stability and consistency of measures (Kroll, 1966). Stability is a measure of resistance to influence from repeated testing and can be assessed with a repeated measures analysis of variance (ANOVA). Consistency shows that the same factor is being measured on different occasions. Intraclass reliability is a technique that assesses consistency via analysis of variance (Lindquist, 1953). The mean square values for the different sources of error are used to calculate the error terms which is described by Lindquist (1953) in detail. This technique is preferred over interclass Pearson product-moment correlation in its ability to distinguish the various sources of error within an observed score (Kroll, 1966). Intraclass reliability is expressed as follows:

$$R = \frac{\sigma^2 \text{ True Score}}{\sigma^2 \text{ True Score} + \sigma^2 \text{ Error Due to Trials} + \sigma^2 \text{ Error Due to Days}}$$

FIGURE 2

REPLICABILITY OF PREP WAVEFORM ON DAY 1

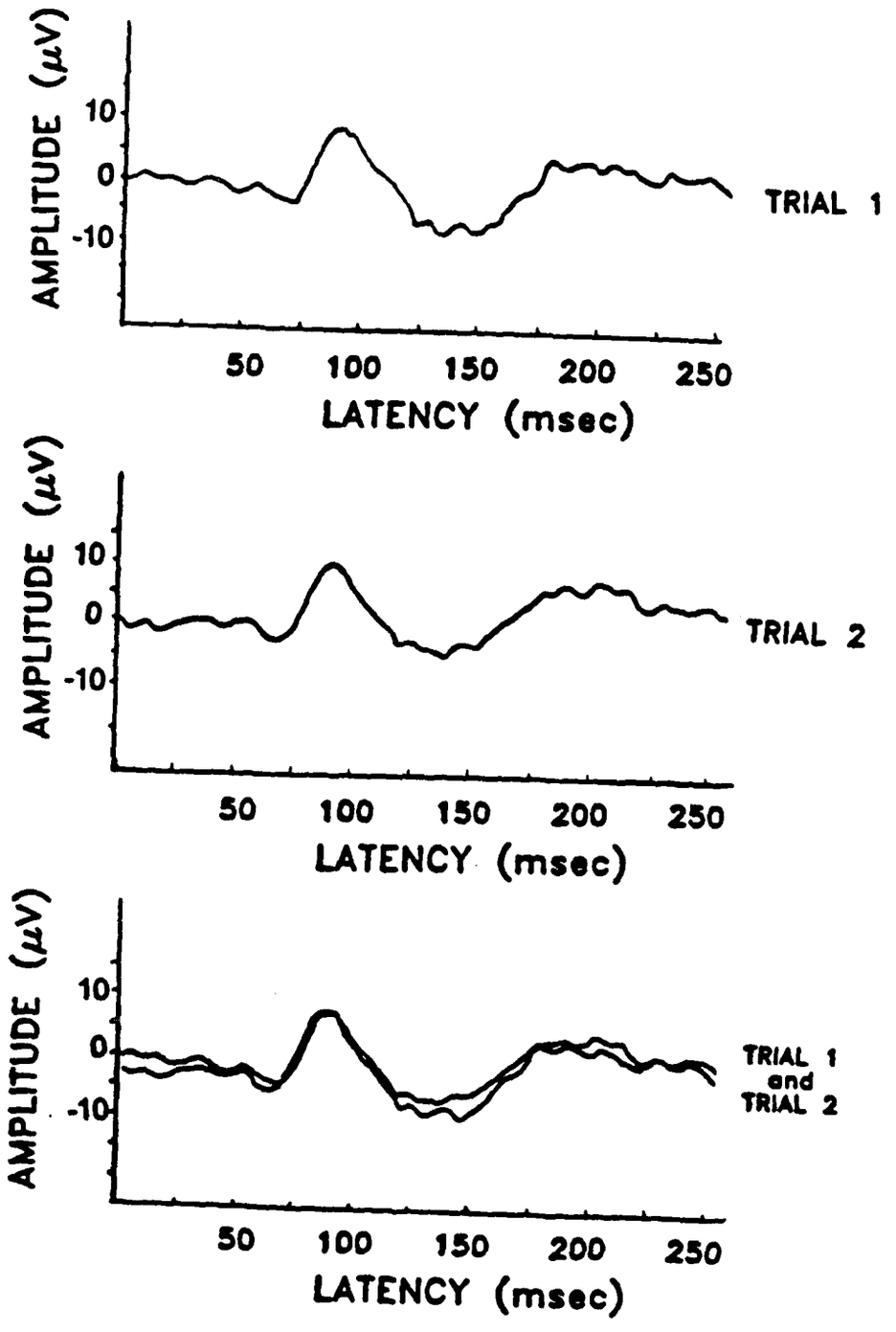
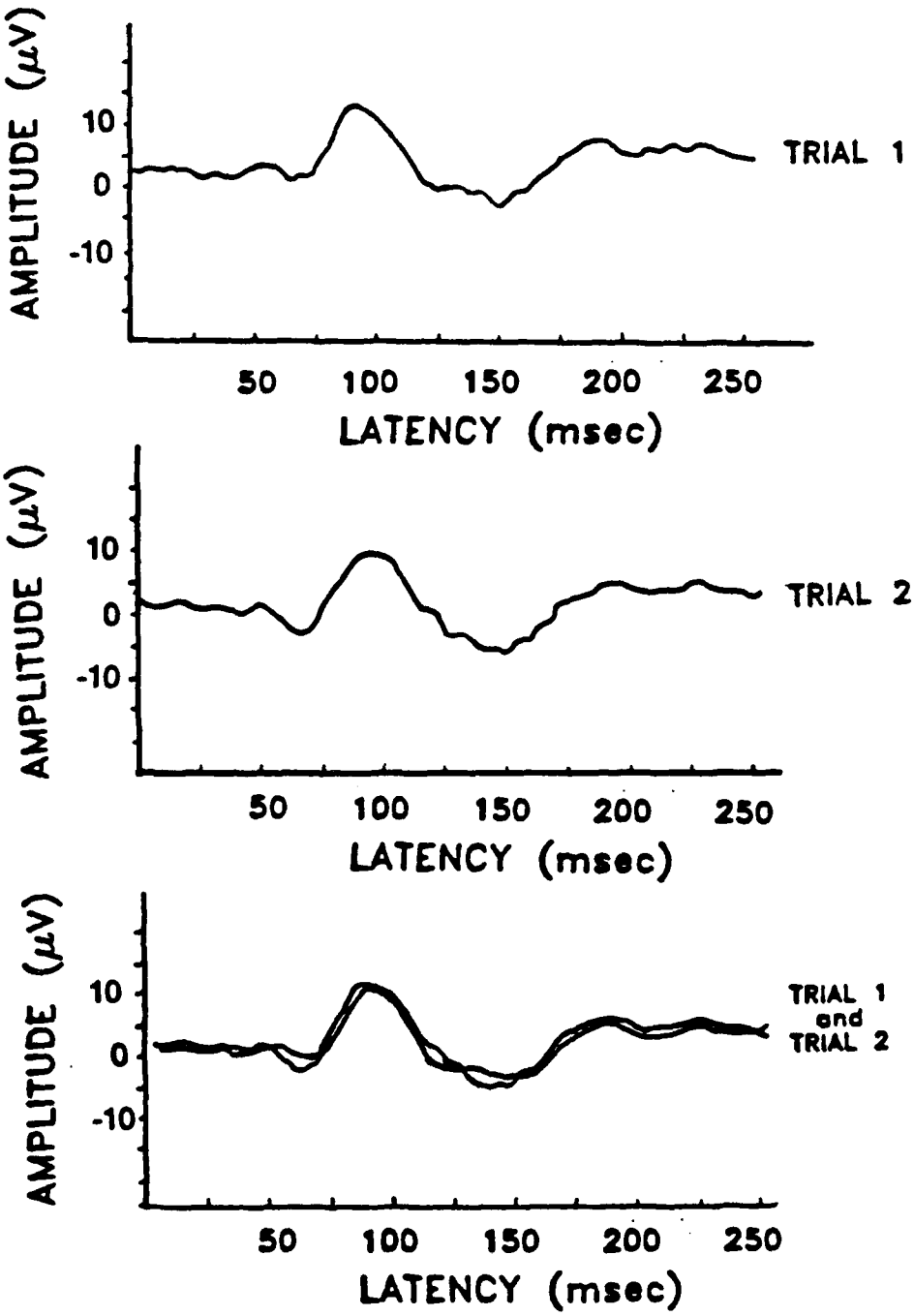


FIGURE 3

REPLICABILITY OF PREP WAVEFORM ON DAY 2



Results

Figure 1 shows a standard PREP wave recorded during this study. Key wave components ($N\overline{75}$, $P\overline{100}$, $N\overline{145}$) are noted. Amplitude $N\overline{75}$-$P\overline{100}$ is from the lowest point of the $N\overline{75}$ valley to the apex of the $P\overline{100}$ peak. The same peak to valley measurement is used for amplitude $P\overline{100}$ to $N\overline{145}$. Figures 2 and 3 illustrate a clear, representative example of the reproducibility of the PREP waveform of one subject (female) on two different days. Trials 1 and 2 in Figures 2 and 3 are each shown separately as well as superimposed on one another to demonstrate the reproducibility of the waves.

Stability of Measures

The ANOVA analysis for stability showed only one significant treatment effect on latency. For wave $P\overline{100}$ from recording site F_{Pz}-O_1 on the left eye; ($F(1,33) = 5.94$, $p < .02$), Day 2's latency was significantly longer than Day 1's. There were significant day effects for both amplitude measures from both eyes $N\overline{75}$-$P\overline{100}$ and $P\overline{100}$-$N\overline{145}$ for recording site F_{Pz}-O_1 only; left eye; ($N\overline{75}$-$P\overline{100}$, $F(1,33) = 5.35$, $p < .03$; $P\overline{100}$-$N\overline{145}$, $F(1,33) = 7.32$, $p < .01$) right eye; ($N\overline{75}$-$P\overline{100}$, $F(1,33) = 7.54$, $p < .01$; $P\overline{100}$-$N\overline{145}$, $F(1,33) = 6.01$, $p < .02$). Amplitudes were also greater on Day 2. These were the only treatment effects observed for amplitude. Actual latencies and amplitudes for the different waves are listed in Tables 1 through 6 with respect to stimulated eye (left or right) and recording site (F_{Pz}-O_1, O_2, or $O_{2'}$).

Consistency of Measures

Consistency for PREP latencies are listed in Table 7. Reliability scores for PREP latencies for waves $\overline{P100}$ and $\overline{N145}$ range from .44 to .79. Reliability for wave $\overline{N75}$ was much lower ranging from .12 to .45.

Reliability scores for amplitudes (Table 8) ranged from .48 to .85 for the different recording sites.

Gender Effects

There were significant differences between males and females in the $\overline{P100}$ wave for both eyes and for all recording sites: left eye; (F_{Pz}-O_1, $F(1,33) = 8.81$, $p < .01$; F_{Pz}-O_2, $F(1,33) = 6.54$, $p < .01$; and F_{Pz}-O_2, $F(1,33) = 7.78$, $p < .01$), and right eye; (F_{Pz}-O_1, $F(1,33) = 4.61$, $p < .04$; F_{Pz}-O_2, $F(1,33) = 7.70$, $p < .01$; and F_{Pz}-O_2, $F(1,33) = 7.60$, $p < .01$). Males had longer latencies in all cases than females. Latency values for the $\overline{P100}$ wave are listed in Tables 1 through 6. There were no gender differences for either $\overline{N75}$ or $\overline{N145}$ latencies for any recording sites for either eye.

Gender effects existed on amplitude for both eyes at all three recording sites for both waves ($\overline{N75}$-$\overline{P100}$ and $\overline{P100}$-$\overline{N145}$). Where significant differences existed between males and females, females always exhibited greater amplitude. There were significant differences for wave $\overline{N75}$-$\overline{P100}$ for right eye; (F_{Pz}-O_1, $F(1,33) = 5.55$, $p < .02$; F_{Pz} -O_2, $F(1,33) = 12.62$, $p < .01$; F_{Pz}-O_2, $F(1,33) = 7.57$, $p < .01$), and left eye; (F_{Pz}-O_1, $F(1,33) = 5.28$, $p < .01$; F_{Pz}-O_2, $F(1,33) = 6.61$, $p < .01$). The only significant difference for wave $\overline{P100}$-$\overline{N145}$ was for right eye; (F_{Pz}-O_1, $F(1,33) = 4.91$, $p < .03$).

TABLE 1
Latencies and Amplitudes for Recording
Site F_{Pz}-O_1 for the Left Eye

		GENDER					
		MALES			FEMALES		
		MEAN	±	S.D.	MEAN	±	S.D.
LATENCY							
	Wave $\overline{N75}$	74.94	±	7.48	71.61	±	3.90
**	Wave $\overline{P100}$	103.71	±	7.45	97.18	±	4.88
	Wave $\overline{N145}$	141.88	±	11.64	138.19	±	13.92
AMPLITUDE							
*	AMP $\overline{N75}$-$\overline{P100}$	5.31	±	2.64	7.32	±	2.52
	AMP $\overline{P100}$-$\overline{N145}$	6.68	±	3.38	8.50	±	3.26

		DAY					
		DAY 1			DAY 2		
		MEAN	±	S.D.	MEAN	±	S.D.
LATENCY							
	Wave $\overline{N75}$	72.42	±	5.18	75.36	±	6.20
*	Wave $\overline{P100}$	100.24	±	5.41	103.06	±	6.96
	Wave $\overline{N145}$	140.84	±	11.69	140.61	±	13.88
AMPL..UDE							
*	AMP $\overline{N75}$-$\overline{P100}$	5.47	±	2.17	6.41	±	3.02
**	AMP $\overline{P100}$-$\overline{N145}$	6.79	±	2.94	7.72	±	3.87

---

* $p < .05$
** $p < .01$

TABLE 2
Latencies and Amplitudes for Recording
Site F_{Pz}-O_z for the Left Eye

	GENDER					
	MALES			FEMALES		
	MEAN	±	S.D.	MEAN	±	S.D.
LATENCY						
Wave $\overline{N75}$	74.95	±	5.22	73.13	±	2.67
** Wave $\overline{P100}$	102.15	±	6.46	97.08	±	5.29
Wave $\overline{N145}$	140.72	±	10.09	138.51	±	11.49
AMPLITUDE						
** AMP $\overline{N75}$-$\overline{P100}$	7.47	±	3.01	10.12	±	3.05
AMP $\overline{P100}$-$\overline{N145}$	9.23	±	4.39	10.67	±	3.80

	DAY					
	DAY 1			DAY 2		
	MEAN	±	S.D.	MEAN	±	S.D.
LATENCY						
Wave $\overline{N75}$	72.81	±	4.41	74.94	±	3.48
Wave $\overline{P100}$	99.35	±	5.31	101.75	±	6.43
Wave $\overline{N145}$	137.66	±	9.49	139.25	±	12.09
AMPLITUDE						
AMP $\overline{N75}$-$\overline{P100}$	8.11	±	2.96	8.49	±	3.08
AMP $\overline{P100}$-$\overline{N145}$	9.74	±	4.57	9.62	±	3.83

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* $p < .05$
** $p < .01$

TABLE 3
Latencies and Amplitudes for Recording
Site F_{Pz}-O_2 for the Left Eye

	GENDER					
	MALES			FEMALES		
	MEAN	±	S.D.	MEAN	±	S.D.
LATENCY						
Wave $\overline{N75}$	75.13	±	5.64	72.16	±	3.39
** Wave $\overline{P100}$	103.50	±	7.35	97.43	±	5.75
Wave $\overline{N145}$	143.09	±	10.39	138.92	±	15.36
AMPLITUDE						
AMP $\overline{N75}$-$\overline{P100}$	5.88	±	2.78	7.84	±	3.47
AMP $\overline{P100}$-$\overline{N145}$	7.60	±	4.14	9.39	±	4.67

	DAY					
	DAY 1			DAY 2		
	MEAN	±	S.D.	MEAN	±	S.D.
LATENCY						
Wave $\overline{N75}$	73.86	±	5.06	74.54	±	3.98
Wave $\overline{P100}$	100.61	±	6.26	102.57	±	6.89
Wave $\overline{N145}$	140.38	±	12.57	141.30	±	13.67
AMPLITUDE						
AMP $\overline{N75}$-$\overline{P100}$	6.48	±	2.92	6.51	±	3.07
AMP $\overline{P100}$-$\overline{N145}$	8.14	±	4.14	8.18	±	4.55

---

* $p < .05$
** $p < .01$

TABLE 4
Latencies and Amplitudes for Recording
Site F_{P2}-O_1 for the Right Eye

	GENDER					
	MALES			FEMALES		
	MEAN	±	S.D.	MEAN	±	S.D.
LATENCY						
Wave N75	74.74	±	7.75	72.43	±	6.08
* Wave P100	103.89	±	7.39	98.94	±	7.26
Wave N145	140.31	±	10.24	139.49	±	12.65
AMPLITUDE						
* AMP N75-P100	5.12	±	2.06	6.81	±	2.61
* AMP P100-N145	6.18	±	2.65	8.49	±	3.91

	DAY					
	DAY 1			DAY 2		
	MEAN	±	S.D.	MEAN	±	S.D.
LATENCY						
Wave N75	72.46	±	7.91	75.58	±	6.54
Wave P100	102.12	±	7.78	102.54	±	6.91
Wave N145	140.24	±	10.24	139.87	±	11.57
AMPLITUDE						
** AMP N75-P100	5.17	±	1.84	6.14	±	2.63
* AMP P100-N145	6.50	±	2.66	7.32	±	3.44

---

* $p < .05$
** $p < .01$

TABLE 5
Latencies and Amplitudes for Recording
Site F_{pz}-O_z for the Right Eye

	GENDER					
	MALES			FEMALES		
	MEAN	±	S.D.	MEAN	±	S.D.
LATENCY						
Wave $\overline{N75}$	74.23	±	5.60	73.80	±	3.33
** Wave $\overline{P100}$	102.01	±	5.19	97.55	±	4.33
Wave $\overline{N145}$	141.43	±	8.51	138.10	±	7.97
AMPLITUDE						
** AMP $\overline{N75}$-$\overline{P100}$	6.99	±	2.57	10.44	±	3.72
AMP $\overline{P100}$-$\overline{N145}$	8.77	±	3.69	11.62	±	5.35

	DAY					
	DAY 1			DAY 2		
	MEAN	±	S.D.	MEAN	±	S.D.
LATENCY						
Wave $\overline{N75}$	73.14	±	5.42	75.04	±	4.34
Wave $\overline{P100}$	100.17	±	5.40	101.04	±	4.44
Wave $\overline{N145}$	140.39	±	8.66	140.38	±	8.01
AMPLITUDE						
AMP $\overline{N75}$-$\overline{P100}$	8.01	±	3.20	8.13	±	2.65
AMP $\overline{P100}$-$\overline{N145}$	9.87	±	4.49	9.46	±	3.95

---

* $p < .05$
** $p < .01$

TABLE 6
Latencies and Amplitudes for Recording
Site F_{Pz}-O_2 for the Right Eye

	GENDER					
	MALES			FEMALES		
	MEAN	±	S.D.	MEAN	±	S.D.
LATENCY						
Wave $\overline{N75}$	74.00	±	5.83	71.74	±	3.99
** Wave $\overline{P100}$	103.57	±	7.10	97.40	±	5.70
Wave $\overline{N145}$	143.01	±	9.61	139.77	±	13.02
AMPLITUDE						
** AMP $\overline{N75}$-$\overline{P100}$	5.71	±	2.38	8.40	±	3.75
AMP $\overline{P100}$-$\overline{N145}$	7.19	±	3.53	10.38	±	6.19

	DAY					
	DAY 1			DAY 2		
	MEAN	±	S.D.	MEAN	±	S.D.
LATENCY						
Wave $\overline{N75}$	72.72	±	5.91	78.86	±	4.59
Wave $\overline{P100}$	100.33	±	7.41	101.94	±	6.08
Wave $\overline{N145}$	141.46	±	10.30	142.51	±	11.06
AMPLITUDE						
AMP $\overline{N75}$-$\overline{P100}$	8.01	±	3.20	6.46	±	2.69
AMP $\overline{P100}$-$\overline{N145}$	8.14	±	4.27	8.24	±	4.45

---

* $p < .05$
** $p < .01$

TABLE 7
Intraclass Reliability Analysis for PREP Latencies
for Left and Right Eyes

LATENCIES	σ^2 Trials	σ^2 Days	σ^2 True Score	R
LEFT EYE				
Wave F_{Pz}-O_1				
N75	20.60	38.00	7.98	.12
P100	21.00	11.65	36.99	.53
N145	55.90	34.15	99.39	.52
Wave F_{Pz}-O_2				
N75	10.02	2.85	15.32	.54
P100	8.86	16.33	28.17	.53
N145	20.10	7.95	104.99	.79
Wave F_{Pz}-O_z				
N75	23.90	4.20	12.05	.30
P100	10.21	20.86	34.61	.53
N145	36.70	49.80	102.58	.54
RIGHT EYE				
Wave F_{Pz}-O_1				
N75	31.20	37.70	11.70	.15
P100	15.00	22.50	34.83	.48
N145	52.60	0.15	91.79	.64
Wave F_{Pz}-O_z				
N75	17.52	4.44	14.18	.39
P100	20.62	0.00	18.23	.47
N145	34.70	6.40	48.20	.44
Wave F_{Pz}-O_2				
N75	19.61	2.51	18.13	.45
P100	12.52	8.45	39.93	.66
N145	30.60	10.50	91.90	.69

TABLE 8
Intraclass Reliability Analysis for PREP Amplitudes
For Left and Right Eyes

AMPLITUDES	σ^2 TRIALS	σ^2 DAYS	σ^2 TRUE SCORE	R
LEFT EYE				
Wave F_{Pz}-O_1				
$\overline{N75}$-$\overline{P100}$	1.65	1.89	5.60	.61
$\overline{P100}$-$\overline{N145}$	2.15	1.34	10.42	.75
Wave F_{Pz}-O_z				
$\overline{N75}$-$\overline{P100}$	2.31	2.45	8.12	.63
$\overline{P100}$-$\overline{N145}$	2.39	3.05	14.49	.73
Wave F_{Pz}-O_2				
$\overline{N75}$-$\overline{P100}$	1.64	.89	8.15	.76
$\overline{P100}$-$\overline{N145}$	4.02	.12	16.49	.80
RIGHT EYE				
Wave F_{Pz}-O_1				
$\overline{N75}$-$\overline{P100}$	1.31	2.41	3.50	.48
$\overline{P100}$-$\overline{N145}$	1.36	3.59	7.93	.61
Wave F_{Pz}-O_z				
$\overline{N75}$-$\overline{P100}$	1.70	1.93	8.89	.71
$\overline{P100}$-$\overline{N145}$	2.71	1.78	17.06	.79
Wave F_{Pz}-O_2				
$\overline{N75}$-$\overline{P100}$	2.38	1.03	19.98	.85
$\overline{P100}$-$\overline{N145}$	1.52	1.18	7.94	.75

Discussion

Both latencies and amplitudes have been shown to be stable over time with the exception of recording site F_{Pz}-O_1. Latencies of waves $\overline{P100}$ and $\overline{N145}$ have been shown to be consistent measures from recording sites F_{Pz}-O_z, and F_{Pz}-O_2. Error variances due to trials and days were relatively small compared to true score variance. Because all variances are small, (standard deviations were less than 10% of the means), and there were only two trials each per day on two separate days, the R values are very reasonable and the system can be considered reliable. Furthermore, the demonstrated stability over time for recording sites F_{Pz}-O_z, and F_{Pz}-O_2, indicate these measures may be held in confidence when testing for PREPs in this laboratory. Most of the variance was due to inter-subject differences. While amplitudes vary much more than latencies, amplitudes were reliable at all recording sites except F_{Pz}-O_1, where instability was evidenced over days for amplitude as well as for latencies.

The following reasons have been suggested as causes for small amounts of variability in waves: 1) small changes in arousal that were unnoticed during testing, 2) subjects closing their eyes or losing focus on the dot before being alerted by the technician, 3) pupil size, 4) body temperature, or 5) small differences in electrode placement (Osken, Chiappa, and Gill, 1987).

Females have previously been reported to have shorter PREP wave latencies probably due to smaller brain and head sizes (Celesia, 1985; Halliday and McDonald, 1981; Shearer and Dustman, 1980; and Stockard, Hughes, and Sharbrough, 1979). In agreement with these findings, our

laboratory found significant differences for the $\overline{P100}$ latencies between males and females regardless of recording site or eye tested. Females always had shorter latencies. However, males tended to show a much greater variability in their latency measures. The differences may be because of greater variability in head sizes of males compared to females. In addition, amplitudes for females were significantly greater, probably due to a shorter distance from the electrical potential generator to the recording site.

Finally, all our values on waves $\overline{P100}$ fall within the 2.5 standard deviation units of our reference laboratory 89.55 - 115.08 msec (Colon, et al., 1983 and Chiappa, 1983). Therefore, the values for the different recording sites in Tables 1-6 will serve as the normative values in future studies conducted in USARIEM's evoked potential laboratory. Separate normative values for males and females will be used because of the significant differences observed on wave $\overline{P100}$.

Recording site F_{pz}-O_z has been shown to be the most reliable PREP site. It is recommended that PREP research in this laboratory utilize this site using Grand Averages (Nicolet Biomedical Instruments, 1987). Grand Averages combine two or more PREP recordings into one wave, to give the equivalent of 200 averages. This procedure is done internally by the Pathfinder to produce a cleaner, more representative wave. Recordings should only be combined into Grand Averages when there is high replication in the separate waveform components. Recording site F_{pz}-O_z is the site reported most frequently in the literature regarding PREP research.

Summary

The PREP is emerging as a useful tool to assess functioning of the visual pathway. The Nicolet Pathfinder II is one signal averaging system which can be used to extract the EP from the EEG. This study assessed the ability of our laboratory procedures using the Nicolet Pathfinder II to validate results from other laboratories, measured reliability and provided normative values as reference points for future PREP research to be performed by USARIEM. The system was found to provide stable and consistent recordings of both PREP latencies and amplitudes for sites F_{Pz}-O_z, and F_{Pz}-O_2. Recording site F_{Pz}-O_1 showed some test-retest variability. The study has established PREP norms by gender for the USARIEM laboratory which may be found in Tables 1 through 6.

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